Available online at www.sciencedirect.com
ScienceDirect
European Journal of Obstetrics & Gynecology and Reproductive Biology 128 (2006) 5–9
ejog European Journal of Obstetrics & Gynecology and Reproductive Biology
www.elsevier.com/locate/ejogrb

Interleukin-18 gene promoter polymorphisms and recurrent spontaneous abortion

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Received 26 July 2005; received in revised form 9 January 2006; accepted 8 February 2006

Abstract

Background: IL-18 is a multifunctional cytokine capable of inducing either Th1 or Th2 polarization depending on the immunologic milieu. IL-18 is detected at the materno-fetal interface very soon in early pregnancy. Two polymorphisms in the promoter region of the IL-18 gene at positions of −607 and −137 appear to have functional impacts.
Objective: This study attempts to evaluate the frequency of these two polymorphisms in the IL-18 gene promoter in patients with recurrent spontaneous abortion (RSA) and normal pregnant women.
Subjects and methods: One hundred and two RSA patients and 103 healthy pregnant women were enrolled in this study. Single nucleotide polymorphisms of the IL-18 gene at positions −607 (C/A) and −137 (G/C) were analyzed by the sequence-specific PCR method.
Results: There was no significant association between the allele, genotype, and haplotype frequencies of the two single nucleotide polymorphisms (SNPs) in the IL-18 gene promoter and RSA.
Conclusion: The results of this study showed that IL-18 gene promoter polymorphisms at positions −607 and −137 did not confer susceptibility to RSA in southern Iranian patients.

Keywords: Interleukin-18; Polymorphism; Recurrent spontaneous abortion

1. Introduction

Recurrent spontaneous abortion (RSA), the occurrence of three or more consecutive pregnancy losses in the first trimester, occurs in approximately 1% of pregnant women worldwide. A series of etiological factors responsible for RSA are divided into the embryologically driven causes (abnormal embryonic karyotypes) and maternally driven ones affecting the endometrium and/or placenta (luteal phase defect, hyperprolactinemia, hyperhomocysteinemia, uterine anomalies, coagulation disorders, autoimmune diseases, endocrine disorders, and endometrial defects) [1]. Despite these well-established pathophysiological mechanisms, the exact underlying etiology is still poorly understood in up to 50% of RSA cases. Recent studies shed light on the immune mechanism as a cause of a proportion of these idiopathic pregnancy losses [1–4].

Production of cytokines and the distribution of the immune cells during pregnancy appeared to be critical in pregnancy outcome [1–4]. Interleukin (IL)-18, initially known as an interferon (IFN)-γ inducing factor, is a member of the IL-1 cytokine family, which is produced by a variety of immune and non-immune cells. It is a unique cytokine capable of enhancing either Th1 or Th2 differentiation depending on the immunologic milieu. It also augments the cytotoxic actions of natural killer and CD8+ T cells [5,6].

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0301-2115/$ – see front matter
doi:10.1016/j.ejogrb.2006.02.012